NALFON - fenoprofen calcium capsule
Pedinol Pharmacal Inc.

Cardiovascular Risk

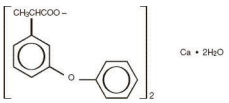
- **NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk (see WARNINGS).**
- **Nalfon® is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).**

Gastrointestinal Risk

- **NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events (see WARNINGS).**

DESCRIPTION

Nalfon® (fenoprofen calcium capsules, USP) is a nonsteroidal, anti-inflammatory, antiarthritic drug. Nalfon capsules contain fenoprofen calcium as the dihydrate in an amount equivalent to 200 mg (0.826 mmol) of fenoprofen. The capsules also contain cellulose, gelatin, iron oxides, silicone, titanium dioxide, and other inactive ingredients.
Chemically, Nalfon is an arylacetic acid derivative.
The structural formula is as follows:



Benzeneacetic acid, α-methyl-3-phenoxy-, calcium salt dihydrate, (±)-
Nalfon is a white crystalline powder that has the structural formula $C_{30}H_{26}CaO_6 \cdot 2H_2O$ representing a molecular weight of 558.65. At 25°C, it dissolves to a 15 mg/mL solution in alcohol (95%). It is slightly soluble in water and insoluble in benzene.
The *p*Ka of Nalfon is a 4.5 at 25°C.

CLINICAL PHARMACOLOGY

Nalfon is a nonsteroidal, anti-inflammatory, antiarthritic drug that also possesses analgesic and antipyretic activities. Its exact mode of action is unknown, but it is thought that prostaglandin synthetase inhibition is involved. Nalfon has been shown to inhibit prostaglandin synthetase isolated from bovine seminal vesicles. Reproduction studies in rats have shown Nalfon to be associated with prolonged labor and difficult parturition when given during late pregnancy. Evidence suggests that this may be due to decreased uterine contractility resulting from the inhibition of prostaglandin synthesis. Its action is not mediated through the adrenal gland.
Fenoprofen shows anti-inflammatory effects in rodents by inhibiting the development of redness and edema in acute inflammatory conditions and by reducing soft-tissue swelling and bone damage associated with chronic inflammation. It exhibits analgesic activity in rodents by inhibiting the writhing response caused by the introduction of an irritant into the peritoneal cavities of mice and by elevating pain thresholds that are related to pressure in edematous hindpaws of rats. In rats made febrile by the subcutaneous administration of brewer's yeast, fenoprofen produces antipyretic action. These effects are characteristic of nonsteroidal, anti-inflammatory, antipyretic, analgesic drugs.
The results in humans confirmed the anti-inflammatory and analgesic actions found in animals. The emergence and degree of erythemic response were measured in adult male volunteers exposed to ultraviolet irradiation. The effects of Nalfon, aspirin, and indomethacin were each compared with those of a placebo. All 3 drugs demonstrated antierythemic activity.
In all patients with rheumatoid arthritis, the anti-inflammatory action of Nalfon has been evidenced by relief of pain, increase in grip strength, and reductions in joint swelling, duration of morning stiffness, and disease activity (as assessed by both the investigator and the patient). The anti-inflammatory action of Nalfon has also been evidenced by increased mobility (i.e., a decrease in the number of joints having limited motion).
The use of Nalfon in combination with gold salts or corticosteroids has been studied in patients with rheumatoid arthritis. The studies, however, were inadequate in demonstrating whether further improvement is obtained by adding Nalfon to maintenance therapy with gold salts or steroids. Whether or not Nalfon used in conjunction with partially effective doses of a corticosteroid has a "steroid-sparing" effect is unknown.
In patients with osteoarthritis, the anti-inflammatory and analgesic effects of Nalfon have been demonstrated by reduction in tenderness as a response to pressure and reductions in night pain, stiffness, swelling, and overall disease activity (as assessed by both the patient and the investigator). These effects have also been demonstrated by relief of pain with motion and at rest and increased range of motion in involved joints.

In patients with rheumatoid arthritis and osteoarthritis, clinical studies have shown Nalfon to be comparable to aspirin in controlling the aforementioned measures of disease activity, but mild gastrointestinal reactions (nausea, dyspepsia) and tinnitus occurred less frequently in patients treated with Nalfon than in aspirin-treated patients. It is not known whether Nalfon causes less peptic ulceration than does aspirin.
In patients with pain, the analgesic action of Nalfon has produced a reduction in pain intensity, an increase in pain relief, improvement in total analgesia scores, and a sustained analgesic effect.
Under fasting conditions, Nalfon is rapidly absorbed, and peak plasma levels of 50 µg/mL are achieved within 2 hours after oral administration of 600 mg doses. Good dose proportionality was observed between 200 mg and 600 mg doses in fasting male volunteers. The plasma half-life is approximately 3 hours. About 90% of a single oral dose is eliminated within 24 hours as fenoprofen glucuronide and 4'-hydroxyfenoprofen glucuronide, the major urinary metabolites of fenoprofen. Fenoprofen is highly bound (99%) to albumin.
The concomitant administration of antacid (containing both aluminum and magnesium hydroxide) does not interfere with absorption of Nalfon.
There is less suppression of collagen-induced platelet aggregation with single doses of Nalfon than there is with aspirin.

INDICATIONS AND USAGE

Carefully consider the potential benefits and risks of Nalfon and other treatment options before deciding to use Nalfon. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see **WARNINGS**).
Nalfon is indicated:

- For relief of mild to moderate pain in adults.
- For relief of the signs and symptoms of rheumatoid arthritis.
- For relief of the signs and symptoms of osteoarthritis.

CONTRAINDICATIONS

Nalfon is contraindicated in patients who have shown hypersensitivity to fenoprofen calcium.
Nalfon should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see **WARNINGS – Anaphylactoid Reactions, and PRECAUTIONS – Preexisting Asthma**).
Nalfon is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS**).
Nalfon is contraindicated in patients with a history of significantly impaired renal function (see **WARNINGS – Advanced Renal Disease**).

WARNINGS

Cardiovascular Effects

Cardiovascular Thrombotic Events
Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may give a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID does increase the risk of serious GI events (see **GI WARNINGS**).

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke (see **CONTRAINDICATIONS**).

Hypertension
NSAIDs, including Nalfon, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including Nalfon, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema
Fluid retention and edema have been observed in some patients taking NSAIDs. Nalfon should be used with caution in patients with fluid retention, compromised cardiac function or heart failure. The possibility of renal involvement should be considered.

Gastrointestinal Effects – Risk of Ulceration, Bleeding, and Perforation
NSAIDs, including Nalfon, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a *prior history of peptic ulcer disease and/or gastrointestinal bleeding* who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population.

To minimize the potential risk for an adverse GI event in patients treated with a NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.

Renal Effects
Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decomposition. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

Advanced Renal Disease
No information is available from controlled clinical studies regarding the use of Nalfon in patients with advanced renal disease. Therefore, treatment with Nalfon is not recommended in patients with advanced renal disease. (see **CONTRAINDICATIONS**).

Anaphylactoid Reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to Nalfon. Nalfon should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs (see **CONTRAINDICATIONS** and **PRECAUTIONS – Preexisting Asthma**). Emergency help should be sought in cases where an anaphylactoid reaction occurs.

Skin Reactions
NSAIDs, including Nalfon, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Pregnancy
In late pregnancy, as with other NSAIDs, Nalfon should be avoided because it may cause premature closure of the ductus arteriosus.

Ocular
Studies to date have not shown changes in the eyes attributable to the administration of Nalfon. However, adverse ocular effects have been observed with other anti-inflammatory drugs. Eye examinations, therefore, should be performed if visual disturbances occur in patients taking Nalfon.

Central Nervous System
Caution should be exercised by patients whose activities require alertness if they experience CNS side effects while taking Nalfon.

Hearing
Since the safety of Nalfon has not been established in patients with impaired hearing, these patients should have periodic tests of auditory function during prolonged therapy with Nalfon.

PRECAUTIONS

General
Nalfon cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
The pharmacological activity of Nalfon in reducing inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, painful conditions.

Hepatic Effects
Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including Nalfon. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice, fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes, have been reported.
A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with Nalfon. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), Nalfon should be discontinued.

Hematological Effects
Anemia is sometimes seen in patients receiving NSAIDs, including Nalfon. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including Nalfon, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia. NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving Nalfon who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.

Preexisting Asthma
Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, Nalfon should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.

Information for Patients
Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.

1. Nalfon, like other NSAIDs, may cause serious CV side effects, such as MI or stroke, which may result in hospitalization and even death. Although serious CV events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, weakness, slurring of speech, and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up (see **WARNINGS, Cardiovascular Effects**).

2. Nalfon, like other NSAIDs, can cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative sign or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up (see **WARNINGS, Gastrointestinal Effects – Risk of Ulceration, Bleeding, and Perforation**).

3. Nalfon, like other NSAIDs, can cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which may result in hospitalization and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible.

4. Patients should promptly report signs or symptoms of unexplained weight gain or edema to their physicians.

5. Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g., nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.

6. Patients should be informed of the signs of an anaphylactoid reaction (e.g. difficulty breathing, swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help (see**WARNINGS**).

7. In late pregnancy, as with other NSAIDs, Nalfon should be avoided because it may cause premature closure of the ductus arteriosus.

Laboratory Tests
Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs should have their CBC and a chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash, etc.) or if abnormal liver tests persist or worsen, Nalfon should be discontinued.

Drug Interactions

ACE-inhibitors
Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.

Aspirin
The coadministration of aspirin decreases the biologic half-life of fenoprofen because of an increase in metabolic clearance that results in a greater amount of hydroxylated fenoprofen in the urine. Although the mechanism of interaction between fenoprofen and aspirin is not totally known, enzyme induction and displacement of fenoprofen from plasma albumin binding sites are possibilities. As with other NSAIDs, concomitant administration of fenoprofen calcium and aspirin is not generally recommended because of the potential of increased adverse effects.

Diuretics
Clinical studies, as well as post marketing observations, have shown that Nalfon can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure (see **WARNINGS, Renal Effects**), as well as to assure diuretic efficacy.

Lithium
NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Methotrexate
NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Warfarin
The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

Phenobarbital
Chronic administration of phenobarbital, a known enzyme inducer, may be associated with a decrease in the plasma half-life of fenoprofen. When phenobarbital is added to or withdrawn from treatment, dosage adjustment of Nalfon may be required.

Plasma Protein Binding
In vitro studies have shown that fenoprofen, because of its affinity for albumin, may displace from their binding sites other drugs that are also albumin bound, and this may lead to drug interactions. Theoretically, fenoprofen could likewise be displaced. Patients receiving hydantoins, sulfonamides, or sulfonylureas should be observed for increased activity of these drugs and, therefore, signs of toxicity from these drugs.

Drug/Laboratory Test Interactions
Amerlex-M kit assay values of total and free triiodothyronine in patients receiving Nalfon have been reported as falsely elevated on the basis of a chemical cross-reaction that directly interferes with the assay. Thyroid-stimulating hormone, total thyroxine, and thyrotropin-releasing hormone response are not affected.

Pregnancy

Teratogenic Effects

Pregnancy Category C
Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women. Nalfon should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects
Because of the known effects of nonsteroidal anti-inflammatory drugs on the fetal cardiovascular system (closure of ductus arteriosus), use during pregnancy (particularly late pregnancy) should be avoided.

Labor and Delivery
In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. The effects of Nalfon on labor and delivery in pregnant women are unknown.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Nalfon, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Safety and effectiveness in pediatric patients below the age of 18 have not been established.

Geriatric Use
As with any NSAIDs, caution should be exercised in treating the elderly (65 years and older).

ADVERSE REACTIONS
During clinical studies for rheumatoid arthritis, osteoarthritis, or mild to moderate pain and studies of pharmacokinetics, complaints were compiled from a checklist of potential adverse reactions, and the following data emerged. These encompass observations in 6,786 patients, including 188 observed for at least 52 weeks. For comparison, data are also presented from complaints received from the 266 patients who received placebo in these same trials. During short-term studies for analgesia, the incidence of adverse reactions was markedly lower than that seen in longer-term studies.

INCIDENCE GREATER THAN 1%

Probable Causal Relationship
Digestive System—During clinical trials with Nalfon, the most common adverse reactions were gastrointestinal in nature and occurred in 20.8% of patients receiving Nalfon as compared to 16.9% of patients receiving placebo. In descending order of frequency, these reactions included dyspepsia (10.3% Nalfon, vs. 2.3%, placebo), nausea (7.7% vs. 7.1%), constipation (7% vs. 1.5%), vomiting (2.6% vs. 1.9%), abdominal pain (2% vs. 1.1%), and diarrhea (1.8% vs. 4.1%). The drug was discontinued because of adverse gastrointestinal reactions in less than 2% of patients during premarketing studies.

Nervous System—The most frequent adverse neurologic reactions were headache (8.7% vs. 7.5%) and somnolence (8.5% vs. 6.4%). Dizziness (6.5% vs. 5.6%), tremor (2.2% vs. 0.4%), and confusion (1.4% vs. none) were noted less frequently. Nalfon was discontinued in less than 0.5% of patients because of these side effects during premarketing studies.

Skin and Appendages—Increased sweating (4.6% vs. 0.4%), pruritus (4.2% vs. 0.8%), and rash (3.7% vs. 0.4%) were reported. Nalfon was discontinued in about 1% of patients because of an adverse effect related to the skin during premarketing studies.

Special Senses—Tinnitus (4.5% vs. 0.4%), blurred vision (2.2% vs. none), and decreased hearing (1.6% vs. none) were reported. Nalfon was discontinued in less than 0.5% of patients because of adverse effects related to the special senses during premarketing studies.

Cardiovascular—Palpitations (2.5% vs. 0.4%). Nalfon was discontinued in about 0.5% of patients because of adverse cardiovascular reactions during premarketing studies.

Miscellaneous—Nervousness (5.7% vs. 1.5%), asthenia (5.4% vs. 0.4%), peripheral edema (5.0% vs. 0.4%), dyspnea (2.8% vs. none), fatigue (1.7% vs. 1.5%), upper respiratory infection (1.5% vs. 5.6%), and nasopharyngitis (1.2% vs. none).

INCIDENCE LESS THAN 1%

Probable Causal Relationship
The following adverse reactions, occurring in less than 1% of patients, were reported in controlled clinical trials and voluntary reports made since Nalfon was initially marketed. The probability of a causal relationship exists between Nalfon and these adverse reactions:

Digestive System—Gastritis, peptic ulcer with/without perforation, gastrointestinal hemorrhage, anorexia, flatulence, dry mouth, and blood in the stool. Increases in alkaline phosphatase, LDH, SGOT, jaundice, and cholestatic hepatitis were observed (see **PRECAUTIONS**).

Genitourinary Tract—Renal failure, dysuria, cystitis, hematuria, oliguria, azotemia, anuria, interstitial nephritis, nephrosis, and papillary necrosis (see **WARNINGS**).

Hypersensitivity—Angioedema (angioneurotic edema).

Hematologic—Purpura, bruising, hemorrhage, thrombocytopenia, hemolytic anemia, aplastic anemia, agranulocytosis, and pancytopenia.

Miscellaneous—Anaphylaxis, urticaria, malaise, insomnia, and tachycardia.

INCIDENCE LESS THAN 1%

Causal Relationship Unknown
Other reactions, reported either in clinical trials or spontaneously, occurred in circumstances in which a causal relationship could not be established. However, with these rarely reported reactions, the possibility of such a relationship cannot be excluded. Therefore, these observations are listed to alert the physician.

Skin and Appendages—Exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, and alopecia.

Digestive System—Aphthous ulcerations of the buccal mucosa, metallic taste, and pancreatitis.

Cardiovascular—Atrial fibrillation, pulmonary edema, electrocardiographic changes, and supraventricular tachycardia.

Nervous System—Depression, disorientation, seizures, and trigeminal neuralgia.

Special Senses—Burning tongue, diplopia, and optic neuritis.

Miscellaneous—Personality change, lymphadenopathy, mastodynia, and fever.

OVERDOSAGE

Signs and Symptoms
Symptoms of overdose appear within several hours and generally involve the gastrointestinal and central nervous systems. They include dyspepsia, nausea, vomiting, abdominal pain, dizziness, headache, ataxia, tinnitus, tremor, drowsiness, and confusion. Hyperpyrexia, tachycardia, hypotension, and acute renal failure may occur rarely following overdose. Respiratory depression and metabolic acidosis have also been reported following overdose with certain NSAIDs.

Treatment
To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the Physicians' Desk Reference (PDR). In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.
Alkalinization of the urine, forced diuresis, peritoneal dialysis, hemodialysis, and charcoal hemoperfusion do not enhance systemic drug elimination.

DOSAGE AND ADMINISTRATION

Carefully consider the potential benefits and risks of Nalfon and other treatment options before deciding to use Nalfon. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see **WARNINGS**).

After observing the response to initial therapy with Nalfon, the dose and frequency should be adjusted to suit an individual patient's needs.

Analgesia

For the treatment of mild to moderate pain, the recommended dosage is 200 mg given orally every 4 to 6 hours, as needed.

Rheumatoid Arthritis and Osteoarthritis

For the relief of rheumatoid arthritis or osteoarthritis the recommended dose is 300 to 600 mg given orally, 3 or 4 times a day. The dose should be tailored to the needs of the patient and may be increased or decreased depending on the severity of the symptoms. Dosage adjustments may be made after initiation of drug therapy or during exacerbations of the disease. Total daily dosage should not exceed 3,200 mg.

Nalfon may be administered with meals or with milk. Although the total amount absorbed is not affected, peak blood levels are delayed and diminished.

Patients with rheumatoid arthritis generally seem to require larger doses of Nalfon than do those with osteoarthritis. The smallest dose that yields acceptable control should be employed.

Although improvement may be seen in a few days in many patients, an additional 2 to 3 weeks may be required to gauge the full benefits of therapy.

HOW SUPPLIED

Nalfon® (fenoprofen calcium capsules, USP) are available in:

The **200 mg**[1] capsule is opaque yellow No. 97 cap and opaque white body, imprinted with "RX681" on the cap and body.

NDC 0884-6600-10 Bottles of 100

Preserve in well-closed containers.

Store at 20° - 25° C (68° - 77° F). (See USP Controlled Room Temperature).

1Equivalent to fenoprofen.

ATTENTION DISPENSER: Accompanying Medication Guide must be dispensed with this product.

Nalfon® (nal-fon) capsules

generic name: fenoprofen calcium

Medication Guide For Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

(See the end of this Medication Guide for a list of prescription NSAID medicines.)

What is the most important information I should know about medicines called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?

NSAID medicines may increase the chance of a heart attack or stroke that can lead to death. This chance increases:

- with longer use of NSAID medicines
- in people who have heart disease

NSAID medicines should never be used right before or after a heart surgery called a "coronary artery bypass graft (CABG)."

NSAID medicines can cause ulcers and bleeding in the stomach and intestines at any time during treatment. Ulcers and bleeding:

- can happen without warning symptoms
- may cause death

The chance of a person getting an ulcer or bleeding increases with:

- taking medicines called "corticosteroids" and "anticoagulants"
- longer use
- smoking
- drinking alcohol

• older age

• having poor health

NSAID medicines should only be used:
• exactly as prescribed

• at the lowest dose possible for your treatment

• for the shortest time needed

What are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?
NSAID medicines are used to treat pain and redness, swelling, and heat (inflammation) from medical conditions such as:
• different types of arthritis

• menstrual cramps and other types of short-term pain

Who should not take a Non-Steroidal Anti-Inflammatory Drug (NSAID)?
Do not take an NSAID medicine:
• if you had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine

• for pain right before or after heart bypass surgery

Tell your healthcare provider:
• about all of your medical conditions.

• about all of the medicines you take. NSAIDs and some other medicines can interact with each other and cause serious side effects. **Keep a list of your medicines to show to your healthcare provider and pharmacist.**

• if you are pregnant. **NSAID medicines should not be used by pregnant women late in their pregnancy.**

• if you are breastfeeding. **Talk to your doctor.**

What are the possible side effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)?

Serious side effects include:	**Other side effects include:**
• heart attack	• stomach pain
• stroke	• constipation
• high blood pressure	• diarrhea
• heart failure from body swelling (fluid retention)	• gas
• kidney problems including kidney failure	• heartburn
• bleeding and ulcers in the stomach and intestine	• nausea
• low red blood cells (anemia)	• vomiting
• life-threatening skin reactions	• dizziness
• life-threatening allergic reactions	
• liver problems including liver failure	
• asthma attacks in people who have asthma	

Get emergency help right away if you have any of the following symptoms:
• shortness of breath or trouble breathing

• chest pain

• weakness in one part or side of your body

• slurred speech

• swelling of the face or throat

Stop your NSAID medicine and call your healthcare provider right away if you have any of the following symptoms:

- nausea
- more tired or weaker than usual
- itching
- your skin or eyes look yellow
- stomach pain
- flu-like symptoms
- vomit blood
- there is blood in your bowel movement or it is black and sticky like tar
- unusual weight gain
- skin rash or blisters with fever
- swelling of the arms and legs, hands and feet

These are not all the side effects with NSAID medicines. Talk to your healthcare provider or pharmacist for more information about NSAID medicines.

Other information about Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- Aspirin is an NSAID medicine but it does not increase the chance of a heart attack. Aspirin can cause bleeding in the brain, stomach, and intestines. Aspirin can also cause ulcers in the stomach and intestines.
- Some of these NSAID medicines are sold in lower doses without a prescription (over-the-counter). Talk to your healthcare provider before using over-the-counter NSAIDs for more than 10 days.

NSAID medicines that need a prescription

Generic Name	Tradename
Celecoxib	Celebrex
Diclofenac	Cataflam, Voltaren, Arthrotec (combined with misoprostol)
Diflunisal	Dolobid
Etodolac	Lodine, Lodine XL
Fenoprofen	Nalfon, Nalfon 200
Flurbiprofen	Ansaid
Ibuprofen	Motrin, Tab-Profen, Vicoprofen* (combined with hydrocodone), Combunox (combined with oxycodone)
Indomethacin	Indocin, Indocin SR, Indo-Lemmon, Indomethagan
Ketoprofen	Oruvail
Ketorolac	Toradol
Mefenamic Acid	Ponstel
Meloxicam	Mobic
Nabumetone	Relafen
Naproxen	Naprosyn, Anaprox, Anaprox DS, EC-Naproxyn, Naprelan, Naprapac (copackaged with lansoprazole)
Oxaprozin	Daypro
Piroxicam	Feldene
Sulindac	Clinoril
Tolmetin	Tolectin, Tolectin DS, Tolectin 600

This Medication Guide has been approved by the U.S. Food and Drug Administration.

*****Vicoprofen contains the same dose of ibuprofen as over-the-counter (OTC) NSAIDs, and is usually used for less than 10 days to treat pain. The OTC NSAID label warns that long term continuous use may increase the risk of heart attack or stroke.

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